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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,677	11/19/2003	Sean P. Palecek	960296.00101	9323
26734 7590 08/07/2009 QUARLES & BRADY LLP 33 E. MAIN ST, SUITE 900 P.O. BOX 2113 MADISON, WI 53701-2113				
EXAMINER				
KIM, TAEYOUN				
ART UNIT		PAPER NUMBER		
1651				
NOTIFICATION DATE		DELIVERY MODE		
08/07/2009		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

### Office Action Summary

**Application No.**

10/717,677

**Applicant(s)**

PALECEK ET AL.

**Examiner**

TAEYOON KIM

**Art Unit**

1651

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1, 4-13 and 16-28 is/are pending in the application.
- 4a) Of the above claim(s) 1, 4-12, 25 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13, 16-24, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Response to Amendment/Argument***

Applicant's amendment and response filed on 4/27/2009 has been received and entered into the case.

Claims 2, 3, 14 and 15 are canceled, claims 1, 4-12, 25 and 28 are withdrawn from consideration as being drawn to non-elected subject matter, and claims 13, 16-24, 26 and 27 are pending and have been considered on the merits. All arguments have been fully considered.

Applicant's arguments filed 4/27/2009 have been fully considered but they are not persuasive.

In the response to the previous office action, applicant alleged that Russell would have had no reason to provide, undifferentiated cells in the strain-applying apparatus in their studies of myocytes or fibroblasts because embryonic stem (ES) cells remain undifferentiated in the apparatus. Applicant further asserted that Russell was interested in differentiating myocytes or fibroblasts in specialized substrata by applying mechanical strain to myocytes or fibroblasts, but not to undifferentiated ES cells.

The examiner respectfully disagrees with the applicant's interpretation of Russell et al. First, the teaching of Russell is not about "differentiating" myocytes or fibroblasts. Russell indeed teaches a method to "maintain a differentiated in vivo cell phenotype" by culturing them on microfabricated membranes, and the method can be employed in the in vitro growth of any of a variety of cells including myocardial cells, bone cells, and embryonic stem cells (par. 36, 37, 105-107). Thus, different from the applicant's assertion, the method of Russell is not about to "differentiate" undifferentiated precursor or stem cells to differentiated cells, rather it is a culture

system to maintain the cells already differentiated in vitro particularly for myocytes or fibroblasts, and the culture system can be applied to any cell listed including ES cells for the growth of the cells.

Furthermore, different from applicant's assertion that Russell describes an apparatus that enhances differentiation, not one that maintains or proliferates undifferentiated ES cells, Russell does not teach that the apparatus (Flexercell) induces or enhances differentiation on myocytes or fibroblasts or any other cells in that matter. In fact, as mentioned above, myocytes or fibroblasts are known as differentiated cells, and the culture method using a microfabricated membrane which can be stretched by Flexercell only maintains the cells under the condition similar to in vivo environment rather than "differentiating" myocytes or fibroblasts.

As discussed in the previous office action, the currently claimed invention is interpreted such that the composition comprising ES cells, unconditioned culture medium, flexible solid porous matrix without fibroblast feeder cells, and an apparatus capable of applying periodic strain to the matrix. Russell clearly teach ES cells cultured on a microfabricated membrane (flexible solid porous matrix), and the apparatus (Flexercell). The ES cells of Russell can be grown on the membrane without feeder layers according to Xu et al. Therefore, Russell in view of Xu teach every limitation drawn to the composition.

Applicant's argument is mainly focused on the feature of ES cells being undifferentiated. While applicant emphasizes that ES cells remain "undifferentiated" after the process of using the apparatus applying periodic strain on the matrix, however, the current claims do not particularly teach that the ES cells are the outcome of such periodic strains applied to the cells. The current

claims merely disclose ES cells grown on the matrix in an apparatus. Since Russell teaches to use ES cells on the culture system, the initial ES cells of Russell are inherently undifferentiated.

Even if ES cells are limited to be drawn to those after the application of the periodic strains, it is considered that ES cells before or after such application, although it should be considered as a product-by-process then, should be the same, unless applicant provide evidence that ES cells before the strains differ from ES cells after the strains, or evidence showing the stretch applied by the apparatus of Russell differentiates ES cells.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 13, 16-24, 26 and 27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al. (of the record) in view of Xu et al. (of the record).

Russell et al. teach a hES cell culture composition (see paragraph [0106]) grown on hydrogel matrix (see paragraph [0015]), and an apparatus [Flexercell strain system (FX-3000) and BioFlex plate] (see paragraph [0161]) on which the cells are stretched by a vacuum (see paragraph [0146]). Russell et al. also teach the percentage of strain starting at 5% (see paragraph [0179]) and the frequency of strain or pattern of strain can be readily varied by programming the system (see paragraph [0146]).

Russell et al. do not teach the human embryonic stem cells being grown on Matrigel (flexible porous matrix).

Xu et al. teach a culture of human embryonic stem (hES) cells on Matrigel without fibroblast feeder cells (see Abstract and Fig. 1). Xu et al. also teach undifferentiated hES cells on

Matrigel in non-conditioned ES medium (see Fig. 1J). Xu et al. also teach the undifferentiated hES cells are positive for surface markers such as Oct4 and SSEA-4, and also positive for alkaline phosphatase (see Fig.1 and p.972, left column, 2<sup>nd</sup> paragraph).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute the hydrogel taught by Russell et al. with Matrigel taught by Xu et al. because a person of ordinary skill in the art would recognize Matrigel would be an art-recognized equivalent matrix to the hydrogel for cell culture.

M.P.E.P. §2144.06 states “In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. “This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor.” 209 USPQ at 759.).”

With regard to the limitations drawn to the apparatus of the claims being configured to apply mechanical strain, vacuum pressure, or oscillatory stretching to the matrix and the hES cells, or to exert at least about 5% on the matrix or to stretch at least about 6 times per minutes, the apparatus of Russell et al., Flexercell system, is identical to the claimed apparatus and therefore, the apparatus can be configured to carry out the claimed limitations and thus, it renders the claims obvious.

Furthermore, it would have been obvious for a person of ordinary skill in the art because Russell et al. clearly indicates that varying patterns of strain (e.g. sinusoidal, stepwise, sustained, etc) can be readily programmed using factory-installed protocols using Flexercell strain unit (see paragraph [0146]), thus the various strain rate or the mode of stretching used in the claimed invention are result effective variables and effectively modified by programming the unit. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already

generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); \*\* In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37



CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/  
Primary Examiner, Art Unit 1651